Anesthesiology 2002; 96:795–802

Effects of Recruiting Maneuvers in Patients with Acute Respiratory Distress Syndrome Ventilated with Protective Ventilatory Strategy

Salvatore Grasso, M.D., Luciana Mascia, M.D.,† Monica Del Turco, M.D.,‡ Paolo Malacarne, M.D.,‡ Francesco Giunta, M.D.,§ Laurent Brochard, M.D.,‖ Arthur S. Slutsky, M.D.,# V. Marco Ranieri, M.D.***

Background: **A lung-protective ventilatory strategy with low tidal volume (V_T) has been proposed for use in acute respiratory distress syndrome (ARDS). Alveolar derecruitment may occur during the use of a lung-protective ventilatory strategy and may be prevented by recruiting maneuvers. This study examined the hypothesis that the effectiveness of a recruiting maneuver to improve oxygenation in patients with ARDS would be influenced by the elastic properties of the lung and chest wall.**

Methods: **Twenty-two patients with ARDS were studied during use of the ARDSNet lung-protective ventilatory strategy: V_T was set at 6 ml/kg predicted body weight and positive end-expiratory pressure (PEEP) and inspiratory oxygen fraction (F_{IO_2}) were set to obtain an arterial oxygen saturation of 90–95% and/or an arterial oxygen partial pressure (Pa_{O_2}) of 60–80 mmHg (baseline). Measurements of Pa_{O_2}/F_{IO_2}, static volume–pressure curve, recruited volume (vertical shift of the volume-pressure curve), and chest wall and lung elastance (Est_W and Est_L: esophageal pressure) were obtained on zero end-expiratory pressure, at baseline, and at 2 and 20 min after application of a recruiting maneuver (40 cm H_2O of continuous positive airway pressure for 40 s). Cardiac output (transesophageal Doppler) and mean arterial pressure were measured immediately before, during, and immediately after the recruiting maneuver. Patients were classified *a priori* as responders and nonresponders on the basis of the occurrence or nonoccurrence of a 50% increase in Pa_{O_2}/F_{IO_2} after the recruiting maneuver.**

Results: **Recruiting maneuvers increased Pa_{O_2}/F_{IO_2} by 20 ± 3% in nonresponders (n = 11) and by 175 ± 23% (n = 11; mean ± standard deviation) in responders. On zero end-expiratory pressure, Est_L (28.4 ± 2.2 *vs.* 24.2 ± 2.9 cm H_2O/l) and Est_W (10.4 ± 1.8 *vs.* 5.6 ± 0.8 cm H_2O/l) were higher in nonresponders than in responders ($P < 0.01$). Nonresponders had been ventilated for a longer period of time than responders (7 ± 1 *vs.* 1 ± 0.3 days; $P < 0.001$). Cardiac output and mean arterial pressure decreased by 31 ± 2 and 19 ± 3% in nonresponders and by 2 ± 1 and 2 ± 1% in responders ($P < 0.01$).**

Conclusions: **Application of recruiting maneuvers improves oxygenation only in patients with early ARDS who do not have impairment of chest wall mechanics and with a large potential for recruitment, as indicated by low values of Est_L.**

This article is accompanied by an Editorial View. Please see: Suter PM: Does the advent of (new) low tidal volumes bring the (old) sigh back to the intensive care unit? ANESTHESIOLOGY 2002; 96:783–4.

TRADITIONAL respiratory support for the acute respiratory distress syndrome (ARDS) involves the use of relatively large (10–15 ml/kg) tidal volumes (V_T) to minimize atelectasis and positive end-expiratory pressure (PEEP) to improve arterial oxygenation by means of low inspiratory oxygen fractions (F_{IO_2}).[1] More recently, lung-protective ventilatory strategies have been proposed[2] that are based on the large body of animal data indicating that mechanical ventilation with high V_T is associated with pulmonary injury indistinguishable from ARDS.[3] Cycling end-expiratory collapse with tidal inflation may exacerbate this process.[4] Three recent randomized controlled trials supported these experimental findings, showing that a lung-protective ventilatory strategies based on low V_T is able to decrease markers of pulmonary and systemic inflammation[5] and decrease mortality among patients with ARDS.[6,7]

The American–European consensus conference on ARDS proposed periodic use of recruiting maneuvers to prevent atelectasis when small V_T and/or low PEEP levels are used.[8] Alveolar derecruitment may occur during mechanical ventilation with low V_T, depending on the F_{IO_2}, the regional ventilation/perfusion ratios, and the end-expiratory lung volume.[9,10] On the basis of these recommendations, several studies have investigated the physiologic effects of recruiting maneuvers in patients with ARDS.[6,10–14]

Alterations in respiratory mechanics parallel the time course of ARDS.[15,16] Most patients with early ARDS who have been on the ventilator for only a few days have a static volume pressure (V-P) curve with a marked lower inflection point (LIP) and an upper inflection point (UIP) that occurs well above tidal inflation. By contrast, most patients with late ARDS who have been on the ventilator for several days often have a static V-P curve with an absent LIP and a UIP that occurs within tidal inflation.[15,16]

Impairment of chest wall mechanics in patients with ARDS has been demonstrated[17]; recent studies suggest

* Clinical attending, Servizio di Anestesiologia e Rianimazione, Ospedale Di Venere. † Doctoral student, Dipartimento di Neuroscienze-Sezione di Fisiologia, Universita' di Torino. ‡ Clinical attending, § Professor, and ** Associate Professor, Dipartimento di Chirurgia–Terapia Intensiva, Cattedre di Anestesiologia e Rianimazione, Ospedale S. Chiara, Università di Pisa. ‖ Professor, Service de Réanimation Medicale, Hopital Henri Mondor, Université Paris XII. # Professor, St. Michael's Hospital, University of Toronto.

Received from the Servizio di Anestesiologia e Rianimazione, Ospedale Di Venere, Bari, Italy; Dipartimento di Neuroscienze-Sezione di Fisiologia, Universita di Torino, Torino, Italy; Dipartimento di Chirurgia–Terapia Intensiva, Cattedre di Anestesiologia e Rianimazione, Ospedale S. Chiara, Università di Pisa, Pisa, Italy; Service de Réanimation Medicale, Hopital Henri Mondor, Université Paris XII, Paris, France; and St. Michael's Hospital, University of Toronto, Toronto, Canada. Submitted for publication July 6, 2001. Accepted for publication October 18, 2001. Supported by Consiglio Nazionale delle Ricerche (grant No. 95.00934) and Ministero Universita e Ricerca Scientifica e Tecnologica (MURST)-2001, Rome, Italy. Drs. Grasso and Mascia equally contributed to the study and should therefore both be considered as first authors.

Address reprint requests to Dr. Ranieri: Universita Di Torino, Sezione Di Anestesiologia e Rianinazione Ospedale S. Giovanni Battista, Corso Dogliotti 19, 10126, Torino, Italy. Address electronic mail to: marco.ranieri@unito.it.

that alterations of chest wall mechanics may influence the effects of PEEP on arterial oxygenation[18] and respiratory mechanics.[19]

The current study set out to examine the hypothesis that the effectiveness of the recruiting maneuver to improve oxygenation in patients with ARDS could be influenced by the elastic properties of the lung and chest wall.

Methods

Patient Selection

Twenty-two patients with ARDS were recruited from the intensive care units (ICUs) of the Di Venere, Policlinico (University of Bari), and S. Chiara (University of Pisa) hospitals. The review boards of all three hospitals approved the research protocol, and informed consent was obtained from all patients or next of kin. Inclusion criteria were age >18 yr and diagnosis of ARDS.[20] Exclusion criteria were cardiogenic pulmonary edema (clinically suspected or pulmonary artery occlusion pressure >18 mmHg), history of ventricular fibrillation or tachyarrhythmia, unstable angina or myocardial infarction within the preceding month, preexisting chronic obstructive pulmonary disease, mean arterial pressure (MAP) <65 mmHg (despite attempts to increase blood pressure with fluid and vasopressors, as clinically indicated), anatomic chest wall abnormalities, chest tube with persistent air leak, pregnancy, and intracranial abnormality.

All patients were intubated and ventilated with a Siemens Servo Ventilator 300 (Siemens Elema AB, Solna, Sweden). The investigation was performed in the semirecumbent position after sedation (diazepam, 0.1–0.2 mg/kg, and fentanyl, 2–3 μg/kg) and paralysis (vecuronium, 4–8 mg). A physician not involved in the research aspects of the study was always present to provide patient care.

Study Protocol

Before enrollment, patients were ventilated according to the ARDSNet protective ventilatory strategy: V_T was set at 6 ml/kg predicted body weight; PEEP and F_{IO_2} were set to obtain an arterial oxygen saturation (Sa_{O_2}) value of 90–95% or an arterial oxygen partial pressure (Pa_{O_2}) of 60–80 mmHg (baseline),[7] or both.

At baseline, static inspiratory V-P curves of the respiratory system, chest wall, and lung were obtained with and without PEEP. A recruiting maneuver was then performed by setting the ventilator on the continuos positive airway pressure mode and applying a pressure of 40 cm H_2O for 40 s.[6] After termination of the recruiting maneuver, the previous breathing pattern was reestablished, and measurements of Pa_{O_2}/F_{IO_2} ratio, V-P curve, and respiratory mechanics were obtained 2 min and 20 min after application of the recruiting maneuver.

Measurements

Flow was measured with a heated pneumotachograph (Fleisch no. 2; Fleisch, Lausanne, Switzerland), connected to a differential pressure transducer (Diff-Cap, ±1 cm H_2O; Special Instruments, Nordlingen, Germany) inserted between the Y-piece of the ventilator circuit and the endotracheal tube. The pneumotachograph was linear over the experimental range of flow. Airway opening pressure (Pao) was measured proximal to the endotracheal tube with a pressure transducer (Digima-Clic, ±100 cm H_2O; Special Instruments). Changes in intrathoracic pressure were evaluated by assessment of esophageal pressure (Pes). Esophageal pressure was measured with a thin latex balloon-tipped catheter connected by a polyethylene catheter to a pressure transducer (Digima-Clic, ±100 cm H_2O). The esophageal balloon was filled with 1–1.5 ml of air and correctly positioned by means of an occlusion test performed before sedation and paralysis.[17–19] Transpulmonary pressure was calculated as Pao-Pes. All the variables described above were displayed and collected on a personal computer through a 12-bit analog-to-digital converter board (DAQCard 700; National Instrument, Austin, TX) at a sample rate of 200 Hz (ICU Lab, KleisTEK Engineering, Bari, Italy). Arterial blood samples were analyzed (ABL 330; Radiometer, Copenhagen, Denmark).

The difference between end-expiratory lung volume during mechanical ventilation and the elastic equilibrium volume of the respiratory system on zero end-expiratory pressure (ZEEP) was assessed by reducing respiratory rate to the lowest value possible during a baseline breath, while decreasing PEEP to zero.[21] To standardize volume history, immediately after the prolonged expiration to ZEEP, five consecutive pressure control breaths with an inspiratory pressure of 40 cm H_2O and an inspiratory time of 5 s were applied before reestablishing the baseline ventilatory pattern.[11,14,22] Total PEEP ($PEEP_{tot}$ = applied PEEP plus intrinsic PEEP) of the respiratory system (rs) and of the chest wall (W) were measured as the plateau pressure in Pao and Pes during an end-expiratory occlusion, referenced to their values at the elastic equilibrium point of the respiratory system. $PEEP_{tot}$ applied to the lung (L) was evaluated as $PEEP_{tot,L} = PEEP_{tot,rs} - PEEP_{tot,W}$.[17]

Static inflation V-P curves were obtained by performing single-breath occlusions at different inflating volumes, achieved by changing inflation volumes in random order, and altering the respiratory frequency of the ventilator.[21] Twelve to 15 experimental points were collected.[21] Each occlusion was maintained until an apparent plateau in Pao was observed (3–4 s). The static end-inspiratory pressures of the respiratory system (Pst_{rs}) and chest wall (Pst_W) were measured as the end-inspiratory plateau pressure on Pao and Pes, referenced to their values at the elastic equilibrium volume of the

respiratory system. The static end-inspiratory pressure of the lung (Pst_L) was calculated as the difference between Pst_{rs} and Pst_w. Values of pressures at the upper and lower inflection points of the V-P curve of the lung on ZEEP (UIP_L and LIP_L, respectively) were quantified by means of a step-by-step regression analysis on samples of 4–5 consecutive experimental points, as previously described.[22] Recruited volume at baseline and 2 and 20 min after application of the recruiting maneuver was identified as the upward shift of the V-P curves of the lung, relative to the curve on ZEEP at a fixed pressure (20 cm H_2O).[21]

Static elastance (Est) of the respiratory system was calculated as $Est_{rs} = (Pst_{rs} - PEEP_{cocrs})/V_T$. Static elastance of the chest wall (Est_W) was calculated as $Est_W = (Pst_w - PEEP_{cocw})/V_T$. Static elastance of the lung (Est_L) was calculated as $Est_{rs} - Est_W$.

All patients had a radial artery and central venous catheters for measurements of systemic blood pressure and right atrial pressure. To evaluate the instantaneous effects of the recruiting maneuver on cardiac output, transesophageal continuous-wave Doppler (Doptek-ODM1; Deltex Medical, Chichester, UK) of the descending aorta was measured before and during application of the recruiting maneuver (20–25 s after the onset of the maneuver) and immediately (within 20–25 s) after reestablishment of baseline ventilation. This technique measures blood flow velocity in the descending thoracic aorta, with use of a transducer inserted in the esophagus.[23] Stroke volume may then be derived with an algorithm based on (1) the beat-to-beat maximum velocity–time integral (stroke distance); (2) the cross-sectional area of the descending aorta; and (3) a correction factor that transforms descending aortic blood flow into global cardiac output.[23] The validity of this approach in mechanically ventilated critically ill patients has recently been established.[23]

Patients were defined *a priori* as responders if they had an increase in Pao_2/Fio_2 of ≤50% 2 min after application of the recruiting maneuver; otherwise, they were considered to be nonresponders.[11] On the basis of history, clinical presentation, and microbiologic results,[11,19] ARDS was classified as pulmonary or extrapulmonary by three independent physicians blinded to the study results.

Statistics

Data are expressed as mean ± standard deviation of the mean. Data within groups were compared by analysis of variance for repeated measures with a Bonferroni correction. If significant ($P \geq 0.05$), the values at different experimental conditions were compared with those at baseline with use of a paired *t* test, as modified by Dunnett. Comparisons of data between groups were performed at each experimental condition by the Fisher exact test for categorical variables and the Wilcoxon test for continuous variables. Regression analysis was performed with the least-squares method. Analysis was carried out with the StatView software package (Abacus, Berkeley, CA).

Table 1. Demographic and Clinical Characteristics in Nonresponders and Responders

	Patient	Age	Gender	Underlying Disease	Time on MV (days)
Nonresponders	4	67	M	Pancreatitis	10
	6	38	M	Polytrauma	6
	7	61	F	Peritonitis	7
	8	52	F	Pneumonia	6
	10	28	M	Pneumonia	7
	11	49	F	Peritonitis	6
	14	49	F	Peritonitis	7
	16	63	M	Pneumonia	10
	18	45	F	Peritonitis	5
	21	40	F	Pneumonia	7
	22	30	M	Pneumonia	9
Mean		47			7.1
SD		13			1.5
Responders	1	63	F	Pancreatitis	1
	2	19	M	Polytrauma	1
	3	35	M	Polytrauma	1
	5	25	M	Pneumonia	1
	9	37	F	Pancreatitis	1
	12	41	F	Pneumonia	1
	13	22	F	Pneumonia	1
	15	33	F	Pancreatitis	1
	17	68	M	Pneumonia	1
	19	62	F	Pneumonia	1
	20	62	M	Pneumonia	2
Mean		42			1.0*
SD		18			0.3

Data are mean ± SD.

* $P < 0.001$, Wilcoxon for unpaired data Nonresponders *vs.* Responders.

MV = mechanical ventilation; M = male; F = female.

Results

Two minutes after the application of the recruiting maneuver, Pao_2/Fio_2 increased 20 ± 3% in 11 nonresponders and 175 ± 23% in the responders (11 patients).

Before application of the recruiting maneuver, V_T (6.1 ± 0.1 and 6.0 ± 0.2 ml/kg) and PEEP (9.4 ± 2.2 and 9.1 ± 2.7 cm H_2O) did not differ between nonresponders and responders. Age (47 ± 13 [nonresponders] and 42 ± 18 yr [responders]), sex (five and six males), underlying disease (five and six cases of pulmonary ARDS), and Pao_2/Fio_2 ratio on ZEEP (111 ± 38 *vs.* 105 ± 38) were similar for nonresponders and responders. Time on mechanical ventilation (including time on ventilator in other ICUs before admission to the study centers) was significantly longer ($P < 0.001$) for the nonresponders (table 1).

Values of LIP (8.7 ± 1.2 *vs.* 10.6 ± 1.0 cm H_2O) and UIP (24.2 ± 1.4 *vs.* 27.8 ± 2.2 cm H_2O) on the static V-P

Table 2. Respiratory Mechanics in Nonresponders and Responders on Zero End-expiratory Pressure

		LIP_L	UIP_L	$Est_{,L}$	$Est_{,W}$
	Patient	(cm H_2O)	(cm H_2O)	(cm H_2O/L)	(cm H_2O/L)
Nonresponders	4	8.1	22.8	33.64	9.90
	6	9.1	23.5	29.06	10.70
	7	10.8	25.1	25.11	11.60
	8	6.9	24.5	30.23	9.30
	10	8.7	22.9	27.50	11.50
	11	9.5	26.7	26.00	9.70
	14	8.4	22.7	31.00	10.90
	16	7.6	22.9	28.50	9.30
	18	7.8	24.2	27.90	6.40
	21	10.2	26.4	26.80	12.90
	22	8.5	23.5	31.80	11.90
Mean		8.7	24.2	28.4	10.4
SD		1.2	1.4	2.2	1.8
Responders	1	10.1	27.5	25.67	5.30
	2	9.8	26.6	23.55	6.60
	3	10.7	24.3	28.82	5.20
	5	9.2	26.3	27.92	6.80
	9	10.8	28.8	23.10	5.50
	12	11.5	31.1	27.20	4.30
	13	12.5	25.7	24.50	5.50
	15	10.3	26.9	22.40	6.10
	17	11.8	28.5	19.90	6.20
	19	10.4	30.8	21.90	5.80
	20	9.8	29.8	20.80	4.30
Mean		10.6*	27.8*	24.2*	5.6*
SD		1.0	2.2	2.9	0.8

Data are mean ± SD.

* $P < 0.01$, Wilcoxon for unpaired data Nonresponders *vs.* Responders.

LIP_L = lower inflection point on the static pressure-volume curve of the lung; UIP_L = upper inflection point on the static pressure-volume curve of the lung; $Est_{,L}$ = static elastance of the lung; $Est_{,W}$ = static elastance of the chest wall.

curve of the lung on ZEEP were lower for nonresponders than responders ($P < 0.01$); values of Est_L (28.4 ± 2.2 *vs.* 24.2 ± 2.9 cm H_2O/l) and Est_W (10.4 ± 1.8 *vs.* 5.6 ± 0.8 cm H_2O/l) on ZEEP were higher for nonresponders than responders ($P < 0.01$) (table 2).

Two minutes after the application of the recruiting maneuver, the Pao_2/Fio_2 ratio increased to 180 ± 46 in nonresponders and to 440 ± 60 in responders ($P < 0.001$); 20 min after application of the recruiting maneuver, values of Pao_2/Fio_2 tended to return toward baseline values in both groups (fig. 1, top). Values of Est_L (25.1 ± 2.2 *vs.* 18.9 ± 2.4 cm H_2O/l) at baseline were higher in nonresponders than responders ($P < 0.01$). Two minutes after application of the recruiting maneuver, Est_L decreased to 22.7 ± 1.9 cm H_2O/l in nonresponders (8 ± 3%) and to 14.8 ± 2.3 cm H_2O/l in responders (21 ± 2%) ($P < 0.01$). Est_L returned toward baseline values 20 min after application of the recruiting maneuver in both groups (fig. 1, middle). At baseline, the amount of recruited volume with PEEP was smaller in nonresponders than in responders (199 ± 80 *vs.* 284 ± 37 ml, respectively; $P < 0.01$) and increased after application of the recruiting maneuver to 296 ± 99 ml in nonresponders and 482 ± 80 ml in responders ($P < 0.01$). Twenty minutes after application of the recruiting maneuver, the recruited volume was 263 ± 99 ml in nonresponders and 322 ± 64 ml in responders ($P < 0.01$; fig. 1, bottom).

Physiologic variables in one representative nonresponder and responder are shown in figure 2. Relative to baseline conditions, application of the recruiting maneuver increased the end-expiratory position of the volume and Pes signals only in the responder. At similar V_T, tidal swings of Pes were larger for nonresponders than for responders. Transpulmonary pressure during the sustained inflation was lower in nonresponders than in responders. The reduction in blood pressure and the increase in right atrial pressure after application of the recruiting maneuver were more evident in nonresponders than responders.

On average, heart rate remained unchanged during application of the recruiting maneuver (20–25 s after onset), and cardiac output, stroke volume, and MAP decreased by 31 ± 2, 27 ± 1, and 19 ± 3% in nonresponders and by 2 ± 1, 5 ± 1, and 2 ± 1% in responders, whereas right atrial pressure increased by 19 ± 3 and 2 ± 1%, respectively ($P < 0.01$). All hemodynamic variables returned to baseline values right after ventilation was reestablished after the recruiting maneuver (within 20–30 s; table 3).

Discussion

All ventilatory strategies used to minimize alveolar recruitment–derecruitment and overdistension based on mechanical properties use Pst_{rs} as a surrogate for transpulmonary pressure. However, the lung and the chest wall are in series, and Pst_{rs} equals the sum of Pst_L and Pst_W. Our study shows that a substantial part of the pressure applied to the respiratory system during a recruitment maneuver (to reexpand collapsed alveoli) can be dissipated against a stiff chest wall; we found that the pressure applied to the lung during a fixed recruitment maneuver of 40 cm H_2O was 18.4 ± 3.3 and 28.6 ± 2.1 cm H_2O in nonresponders and responders, respectively.

Matamis *et al.*[15] found that alterations in respiratory mechanics paralleled the evolution of ARDS. In patients on the ventilator for a prolonged period of time and with signs of interstitial fibrosis on a chest radiograph, static V-P curves differed substantially from those observed in patients at an early stage and at the onset of mechanical ventilation. Our study included patients transferred from other ICUs and on mechanical ventilation for 5–10 days (nonresponders) and patients admitted from the emergency department or from the ward and on mechanical ventilation for 1–2 days (responders). Patients in whom

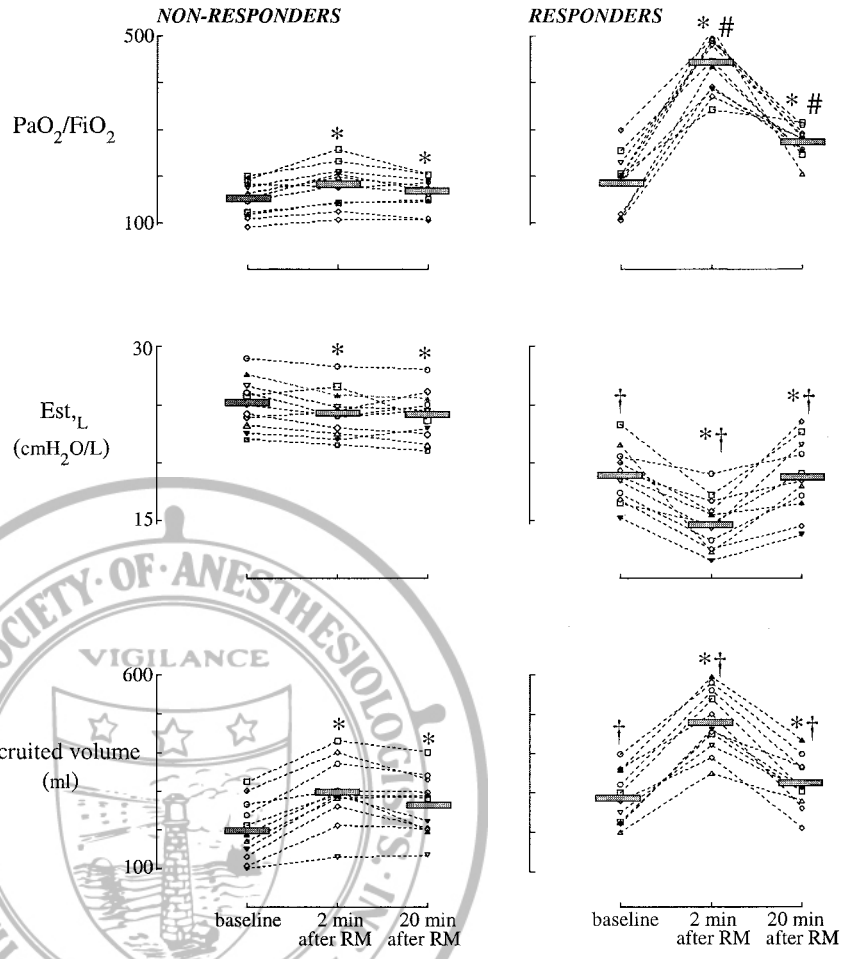

Fig. 1. Individual values of arterial oxygen partial pressure or inspiratory oxygen fraction (Pao_2/Fio_2; *top*) ratio static elastance of the lung (Est_L; *middle*) and recruited volume (*bottom*) during the different experimental conditions in nonresponders and responders (RM = recruiting maneuver; horizontal bars indicate mean values; **P* < 0.01 [analysis of variance for repeated measures with Bonferroni correction *vs.* baseline]; †*P* < 0.05; #*P* < 0.01 [Wilcoxon test, nonresponders *vs.* responders]).

application of a recruiting maneuver caused a substantial improvement in oxygenation were those studied within 1–2 days after initiation of mechanical ventilation. In these patients, Est_L on ZEEP was smaller and LIP_L and UIP_L occurred at higher pressures than in patients studied after 5–10 days of mechanical ventilation. This suggests that the potential for alveolar recruitment with recruiting maneuvers may be reduced in patients with late ARDS.

Recent studies have demonstrated impaired chest wall mechanics in many patients with ARDS consequent to major abdominal surgery[17] and in patients in whom ARDS is caused by extrapulmonary causes.[19] These studies suggested that a great part of the alteration in chest wall mechanics can be explained by abdominal distension.[17,19] It has been shown that in patients with ARDS, chest wall mechanics can be significantly altered by the presence of pleural effusions due to a positive fluid balance.[11,24–27] Mattison *et al.*[26] found that pleural effusions were seen only in patients on the ventilator for 7 ± 1 days, not in patients on the ventilator for only 2 ± 1 days. We found a positive correlation ($R^2 = 0.72$; $P < 0.0001$) between Est_W on ZEEP and days on mechanical ventilation, suggesting that impairment of chest wall mechanics may occur, independently from the underlying disease, because of pleural effusions in patients on the ventilator for a prolonged period of time. Further studies are required to prospectively confirm this hypothesis.

Pelosi *et al.*[11] showed that recruiting maneuvers improved lung mechanics and oxygenation only in patients with extrapulmonary ARDS. In our study, the underlying disease responsible for ARDS did not influence the amount of improvement in arterial oxygenation after application of the recruiting maneuver. The relation between baseline V_T and effects of PEEP and recruiting maneuvers on alveolar recruitment may explain such apparently conflicting data. In the study of Pelosi et al.,[11] V_T and Pst_{rs} during baseline ventilation were 0.56 ± 0.11 L (approximately 10 ml/kg) and 31.6 ± 3.6 cm H_2O, whereas in the present study they were 0.38 ± 0.05 L (6.1 ± 0.1 ml/kg) and 23.3 ± 2.8 cm H_2O, respectively. Several studies have shown that lung mechanics vary considerably with volume history.[28–30] When relatively large V_T (10–12 ml/kg) are used, most alveolar recruitment may occur during tidal inflation, and the potential for further recruitment with PEEP or recruiting maneuvers may be limited.[31] This is confirmed by the observation that alveolar recruitment with PEEP decreases with increasing magnitude of Pst_{rs} on ZEEP.[21,32,33] The larger

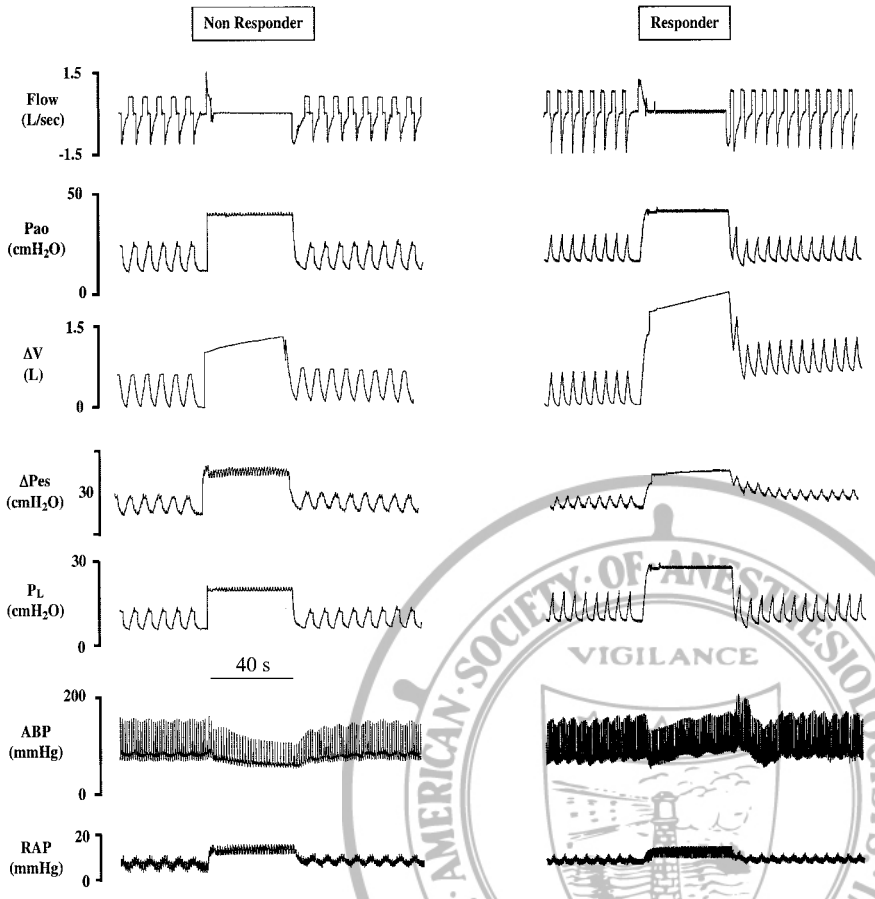

Fig. 2. Physiologic variables in a representative nonresponder and responder before, during, and after application of a recruiting maneuver. From top to bottom: flow, airway opening pressure (Pao), and changes in lung volume (ΔV), esophageal pressure (ΔPes), transpulmonary pressure (P_L), arterial pressure (ABP), and right atrial pressure (RAP).

potential for alveolar recruitment due to the lower V_T used in the current study could therefore explain the improvement in arterial oxygenation with recruiting maneuvers that was also noted in responders with pulmonary ARDS.

Concerns have been voiced about the potential risk of hemodynamic impairment during application of recruiting maneuvers.[34] Our data show that in nonresponders, application of a recruiting maneuver caused a substantial (20–30%) reduction in MAP and cardiac output. The effects of recruiting maneuvers on MAP and cardiac output include a reduced preload due to transmission of Pao to intrathoracic vasculature and/or an increased afterload due to increased lung volume.[35,36] In patients with a stiff chest wall, the degree of Pao transmitted to the pleural space would be larger than in patients with a normal chest wall[35,36]; thus, the decrease in the pressure gradient for venous return (19 ± 3% increase in right atrial pressure) observed in nonresponders during application of recruiting maneuvers might explain the reduction in cardiac output. The more compliant chest wall observed in the responders may induce a smaller transmission of pressure within the thorax, with a larger amount of pressure transmitted to the lung. The smaller decrease in the pressure gradient for venous return (2 ± 1% increase in right atrial pressure) may explain the minimal hemodynamic consequences due to recruiting maneuvers observed in responders.

Table 3. Hemodynamic Variables before, during, and Immediately after Application of a Recruiting Maneuver

	Nonresponders			Responders		
	Before RM	During RM	After RM	Before	During RM	After RM
HR (beats/min)	95 ± 10	103 ± 10	97 ± 7	93 ± 11	98 ± 10	95 ± 9
CO ($L \cdot min^{-1}$)	10.1 ± 0.5	6.1 ± 0.7*	9.45 ± 0.8	10.6 ± 1.7	10.5 ± 1.6	10.8 ± 1.8
SV (ml)	116 ± 15	58 ± 13*	104 ± 12	118 ± 19	110 ± 15	116 ± 20
MAP (mmHg)	85 ± 10	70 ± 5*	86 ± 6	90 ± 6	88 ± 7	91 ± 8
RAP (mmHg)	15.2 ± 1.5	24 ± 2.9*	14.7 ± 0.9	14.2 ± 3.3	16.1 ± 2.7	14.5 ± 5.1

* $P < 0.01$, analysis of variance (ANOVA) for repeated measures with Bonferroni's correction *versus* before RM.

Data are mean ± SD.

RM = recruiting maneuver; HR = heart rate; CO = cardiac output; SV = stroke volume; MAP = mean arterial pressure; RAP = right atrial pressure.

However, cyclic right ventricle afterload occurring during the inspiratory phase has been demonstrated in mechanically ventilated patients.[37] In a recent study, Vieillard-Baron *et al.*[38] found that when Est_W was increased by chest strapping and transpulmonary pressure was reduced by decreasing V_T without changing Pao, the right ventricle was unloaded. In our study the increase in lung volume and transpulmonary pressure during the recruiting maneuver was smaller in nonresponders with worsening hemodynamics (fig. 2). Under these circumstances, the increase in right ventricle afterload would not likely be the mechanism responsible for the reduction in cardiac output and MAP observed during the application of recruiting maneuvers in nonresponders. Echocardiographic evaluation of hemodynamics, not performed in the present study, may confirm these speculations.

One may argue that application of a higher level of continuous positive airway pressure for a longer period of time may have transformed nonresponders into responders. However, the reduction in cardiac output and MAP observed in nonresponders suggests first that the use of more aggressive recruiting maneuvers may worsen the hemodynamic impairment and therefore limit the clinical use of recruiting maneuvers at a pressures higher than 40 cm H_2O, and second, in patients with late ARDS, characterized by a focal distribution of loss of aeration,[39] recruiting maneuvers may provide alveolar recruitment with lung overdistension.[40] Loss of beneficial effects of the recruiting maneuver was observed within 30 min. This may be the result of an insufficient level of PEEP to keep open the alveoli recruited by sustained inflation.[34]

In conclusion, this study demonstrates that application of recruiting maneuvers is successful in improving oxygenation only in patients with early ARDS on the ventilator for 1–2 days and without impairment of chest wall mechanics. In patients ventilated for a longer period of time, the presence of a stiff chest wall and the reduction in blood pressure and cardiac output make the recruiting maneuver ineffective and potentially harmful.

References

1. Bendixen HH, Hedley-White J, Laver MB: Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation: A concept of atelectasis. N Engl J Med 1963; 269:991–6
2. Slutsky AS: Mechanical ventilation. American College of Chest Physicians' Consensus Conference. Chest 1993; 104:1833–59
3. Dreyfuss D, Basset G, Soler P, Saumon G: Intermittent positive-end expiratory pressure hyperventilation with high inflation pressures produces pulmonary microvascular injury in rats. Am Rev Respir Dis 1985; 132:880–4
4. Tremblay L, Valenza F, Ribeiro SP, Li J, Slutsky AS: Injurious ventilatory strategies increases cytokines and c-fos m-RNA expression in an isolated rat lung model. J Clin Invest 1997; 99:944–52
5. Ranieri VM, Suter PM, Tortorella C, De Tullio R, Dayer JM, Brienza A, Bruno F, Slutsky AS: Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: A randomized controlled trial. JAMA 1999; 282:54–61
6. Amato MB, Barbas CS, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi-Filho G, Kairalla RA, Deheinzelin D, Munoz C, Oliveira R, Takagaki TY, Carvalho CR: Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 1998; 338:347–54
7. The Acute Respiratory Distress Syndrome Network: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000; 342:1301–8
8. Artigas A, Bernard GR., Carlet J, Dreyfuss D, Gattinoni L, Hudson L, Lamy M, Marini JJ, Matthay MA, Pinsky MR, R. Spragg, Suter PM, the Consensus Committee: The American-European Consensus Conference on ARDS, part 2. Am J Respir Crit Care Med 1998; 157:1332–47
9. Rothen H, Sporre UB, Engberg G, Wegenius G, Hedenstierna G: Reexpansion of atelectasis during anesthesia: A computed tomographic study. Br J Anaesth 1993; 71:788–95
10. Tusman G, Bohm SH, Vazquez de Anda GF, do Campo JL, Lachmann B: "Alveolar recruitment strategy" improves arterial oxygenation during general anesthesia. Br J Anaesth 1999; 82:8–13
11. Pelosi P, Cadringher P, Bottino N, Panigada M, Carrieri F, Riva E, Lissoni A, Gattinoni L: Sigh in acute respiratory distress syndrome. Am J Respir Crit Care Med 1999; 159: 872–80
12. Foti G, Cereda M, Sparacino ME, De March L, Villa F, Pesenti A: Effects of periodic lung recruitment maneuvers on gas exchange and respiratory mechanics in mechanically ventilated acute respiratory distress syndrome (ARDS) patients. Intensive Care Med 2000; 26:501–7
13. Medoff BD, Harris RS, Kesselman H, Venegas J, Amato MBP, Hess D: Use of recruitment maneuvers and high positive end-expiratory pressure in a patient with acute respiratory distress syndrome. Crit Care Med 2000; 28:1210–6
14. Richard JC, Maggiore SM, Jonson B, Mancebo J, Lemaire F, Brochard L: Influence of tidal volume on alveolar recruitment: Respective role of PEEP and a recruitment maneuver. Am J Respir Crit Care Med 2001; 163:1609–13
15. Matamis D, Lemaire F, Harf A, Brun-Buisson C, Ausquer JC, Atlan G: Total respiratory pressure-volume curves in the adult respiratory distress syndrome. Chest 1984; 86:58–66
16. Blanch LR, Fernandez R, Vallés J, Solé J, Roussos C, Artigas A: Effect of two tidal volumes on oxygenation and respiratory system mechanics during the early stage of adult respiratory distress syndrome. J Crit Care 1994; 17:469–74
17. Ranieri VM, Brienza N, Santostasi S, Puntillo F, Mascia L, Vitale N, Giuliani R, Memeo V, Bruno F, Fiore T, Brienza A, Slutsky AS: Impairment of lung and chest wall mechanics in patients with acute respiratory distress syndrome: Role of abdominal distension. Am J Respir Crit Care Med 1997; 156:1082–91
18. Mergoni M, Martelli A, Volpi A, Primavera S, Zuccoli P, Rossi A: Impact of positive end-expiratory pressure on chest wall and lung pressure-volume curve in acute respiratory failure. Am J Respir Crit Care Med 1997; 156:846–54
19. Gattinoni L, Pelosi P, Suter PM, Pedoto A, Vercesi A, Lissoni A: Acute respiratory distress syndrome caused by pulmonary and extrapulmonary disease. Am J Respir Crit Care Med 1998; 158:3–11
20. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, Lamy M, Legall JR, Morris A, Spragg R: The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 1994; 149:818–24
21. Ranieri VM, Mascia L, Fiore T, Bruno F, Brienza A, Giuliani R: Cardiorespiratory effects of positive end-expiratory pressure during progressive tidal volume reduction (permissive hypercapnia) in patients with acute respiratory distress syndrome. ANESTHESIOLOGY 1995; 83:710–20
22. Brochard L: Respiratory pressure-volume curves, Principles and Practice of Intensive Care Monitoring. Edited by Tobin MJ. New York, McGraw-Hill, 1997, pp 597–616
23. Baltier B, Cholley BP, Belot J-P, Coussaye J-E, Mateo J, Payen DM: Noninvasive monitoring of cardiac output in critically ill patients using transesophageal doppler. Am J Respir Crit Care Med 1998; 158:77–83
24. Aberle DR, Wiener-Kronish JP, Webb WR, Matthay MA: Hydrostatic vs increased permeability pulmonary edema: diagnosis based on radiologic criteria in critically ill patients. Radiology 1988; 168:73–9
25. Katz JA, Zinn SE, Ozanne GM, Fairlay BH: Pulmonary, chest wall and lung-thorax elastances in acute respiratory failure. Chest 1981; 80:304–311
26. Mattison LE, Coppage L, Alderman DF, Herlong JO, Sahn SA: Pleural effusions in the medical ICU: Prevalence, causes and clinical implications. Chest 1997; 111:1018–23
27. Mutoh T, Lamm WJE, Emdree LJ, Hildebrandt J, Albert RK: Volume infusion produces abdominal distension, lung compression, and chest wall stiffening in pigs. J Appl Physiol 1992; 72:575–82
28. Mead J, Collier C: Relation of volume history of lungs to respiratory mechanics in anesthetized dogs. J Appl Physiol 1959; 14:669–78
29. Begin R, Renzetti AD, Bigler AH, Watanabe S: Flow and age dependence of airway closure and dynamic compliance. J Appl Physiol 1975; 38:199–207
30. Bake B, Wood L, Murphy B, Macklem PT, Milic-Emili J: Effect of inspiratory flow rate on regional distribution of inspired gas. J Appl Physiol 1974; 37:8–17
31. Gattinoni L, Pelosi P, Crotti S, Valenza F: Effect of positive end-expiratory pressure on tidal volume and recruitment in adult respiratory distress syndrome. Am J Respir Crit Care Med 1995; 151:1807–14
32. Valta P, Takala J, Eissa NT, Milic-Emili J: Does alveolar recruitment occur with positive end-expiratory pressure in adult respiratory distress syndrome patients? J Crit Care 1993; 8:34–42
33. Goddon S, Fujino Y, Hromi JM, Kacmarek RM: Optimal mean airway pressure during high frequency oscillation. Anesthesiology 2001; 94:862–9

34. Lapinsky SE, Aubin, M, Metha S, Boiteau P, Slutsky AS: Safety and efficacy of a sustained inflation in adults with respiratory failure. Intensive Care Med 1999; 25:1297–301

35. Robotham JL, Takata M, Berman M, Harasawa Y: Ejection fraction revisited. ANESTHESIOLOGY 1991; 74:172–83

36. Romand JA, Shi W, Pinsky MR: Cardiopulmonary effects of positive pressure ventilation during acute lung injury. Chest 1995; 108:1041–8

37. Jardin F, Delorme D, Hardy A, Auvert B, Beauchet A, Bourdarias JP: Reevaluation of hemodynamic consequences of positive pressure ventilation: emphasis on cyclic right ventricular afterloading by mechanical lung inflation. ANESTHESIOLOGY 1990; 72:966–70

38. Vieillard-Baron A, Loubieres Y, Schmitt J-M, Page B, Dubourg O, Jardin F: Cyclic changes in right ventricular output impedance during mechanical ventilation. J Appl Physiol 1999; 87:1644–50

39. Vieira SR, Puybasset L, Lu Q, Richecoeur J, Cluzel P, Coriat P, Rouby JJ: A scanographic assessment of pulmonary morphology in acute lung injury: Significance of the lower inflection point detected on the lung pressure-volume curve. Am J Respir Crit Care Med 1999; 159:1612–23

40. Rouby JJ, Puybasset L, Cluzel P, Richecoeur J, Lu Q, Grenier P: Regional distribution of gas and tissue in acute respiratory distress syndrome: II. Physiological correlations and definition of an ARDS Severity Score. CT ARDS Study Group. Intensive Care Med 2000; 26:1046–56